REMARKS/ARGUMENTS

Applicants respectfully request reconsideration and allowance of this application in view of the amendments above and the following comments. Claims 1-22 were pending. By this Amendment, claims 1-6 and 20-22 have been amended, and claims 7-19 have been canceled without prejudice or disclaimer. It is believed that no new matter has been added. Accordingly, claims 1-6 and 20-22 are pending.

Enablement Rejection

Independent claim 1 has been amended, which now covers a method for determining, ameliorating, and treating endotoxin-mediated cachexia in a human patient, the method comprising the steps of measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient and if any such level is elevated administering to the human patient a therapeutically effective amount of a bile acid selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, dehydrocholic acid, cholic acid, and deoxycholic acid. The enablement rejection seems to be based on the belief that the Examiner did not believe the specification provides enablement in a patient with liver cirrhosis. Support for enablement for the new amended independent claim 1 is shown in the specification (see for example, Figures 8-12). In addition, attached is **Exhibit 1**, which shows an experiment conducted in human patients treating patients with cachexia. Also attached is **Exhibit A**, which is a declaration by the inventor of the claimed invention. As stated in the declaration by the

inventor, the experiment attached as **Exhibit 1** was conducted based on the teachings of the specification.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Claim Rejections under 35 U.S.C. 102(b)

The Examiner rejected claims 1-6 and 19-20 as being anticipated by U.S. Patent 5,639,744, as evidenced by U.S. Patent 4,377595 and/or U.S. Patent 4,898,879.

In order show anticipation, the reference must teach or suggest every element of the claimed invention. These references fail to teach or suggest (as in independent amended claim 1) a method for determining, ameliorating, and treating endotoxin-mediated cachexia in a human patient, the method comprising the steps of measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient and if any such level is elevated administering to the human patient a therapeutically effective amount of a bile acid selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, dehydrocholic acid, cholic acid, and deoxycholic acid. In particular, these references fail to teach or suggest "treating endotoxin-mediated cachexia "and "measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient."

Further, the US Patent '744 is simply directed to a synthetic compound providing amides

between ursodeoxycholic acid (UDCA) and cyclic amino acids, which can be used in therapy of the biliary calculosis of cholesterol and of the pathologies caused by cholestatis. In addition, as being disclosed in the description of US Patent '744, the synthesis of the amide bondage between UDCA and the cyclic amino acid requires an enormous workload. In contrary, the inventive method for ameliorating endotoxin-mediated cachexia teaches that ordinary UDCA is sufficient for the inventive purpose and no further synthesis steps are required. US Patent '595 simply discloses administering of tyrosine and/or phenylalanine and/or other neutral amino acids to a patient with depression to increase the level of norepinephrine which is released into synapses. In US Patent '595 only a vague association of amino acids and cachexia is given and ursodeoxycholic acid is not even mentioned. Similarly, US Patent '879 only discloses a composition for administration to a patient having liver disease, comprising a cysteine free mixture of nonessential and essential amino acids. No cachexia, body wasting or UDCA is also mentioned in US Patent '879.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Claim Rejections under 35 U.S.C. 102(e)

The Examiner rejected claims 1-6 and 19-21 as being anticipated by U.S. Patent 6,251,884 as evidenced by U.S. Patent 4,377,595 and/or U.S. Patent 4,898,879.

U.S. Patent '884 is simply directed to a pharmacologically acceptable composition including a sulfate of UDCA and a pharmacologically acceptable carrier for treating a liver

disease or an inflammatory condition of the gastrointestinal tract in a mammal. However, the synthesis of a UDCA sulfate presumes a huge expense and purification procedure, and is not comparable to the easily realizable method of using common UDCA in the applied invention. Beyond this, no cachexia or endotoxin/LPS or measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient is mentioned in US Patent '884 as in amended independent claim 1. The '595 and '879 patents were previously discussed above. Thus, these references do not anticipate the claimed invention.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Claim Rejections under 35 U.S.C. 102(e)

The Examiner rejected claims 1-6 and 19 as being anticipated by U.S. Patent 5,869,265 as evidenced by U.S. Patent 4,377,595 and/or U.S. Patent 4,898,879.

US Patent '265 only describes a general concept for the treatment of liver cirrhosis, primary biliary cirrhosis, sclerosing cholangits and other diseases which block the normal secretion of bile acids by the liver by the use of UDCA. Beyond this, no cachexia or endotoxin/LPS or measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient is mentioned in US Patent '265 as in amended independent claim 1. The '595 and '879 patents were previously discussed above. Thus, these references do not anticipate the claimed invention.

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Claim Rejections under 35 U.S.C. 103(a)

The Examiner rejected claims 1-6 and 19-22 as being obvious over U.S. Patent 6,251,884 or U.S. Patent 5,869,265 or U.S. Patent 5,639,744 each in view of U.S. Patent 4,377,595 and/or U.S. Patent 4,898,879.

In response, applicants assert that these references individually or combined do not teach or suggest every element of the claimed invention. As stated above, these combined references fail to teach or suggest (as in independent amended claim 1) a method for determining, ameliorating, and treating endotoxin-mediated cachexia in a human patient, the method comprising the steps of measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient and if any such level is elevated administering to the human patient a therapeutically effective amount of a bile acid selected from the group consisting of chenodeoxycholic acid, ursodeoxycholic acid, dehydrocholic acid, cholic acid, and deoxycholic acid. In particular, these combined references fail to teach or suggest 1) treating endotoxin-mediated cachexia; 2) measuring the level of a cytokine or an inflammatory marker or its production in the blood of the patient; and 3) fail to disclose a connection between cachexia, cytokines, LPS, and ursodeoxycholic acid. Furthermore, there is no teaching or suggestion in the reference/s of a connection between cachexia, cytokines, LPS, and ursodeoxycholic acid

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claim 6 as being indefinite

Claim 1 which claim 6 depends on has been amended to cover "bile acid."

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

Rejection of claims 1-6 and 19-22 as containing new matter

One skilled in the art would know that the term "patient" can mean a "human patient." In support of this, documents are attached which show that the term "patient" can mean a "human patient."

It is, therefore, respectfully requested that the Examiner reconsider and withdraw this rejection.

CONCLUSION

Based on the foregoing remarks it is believed that the claim is in condition for allowance. However, should any issue(s) of a minor nature remain, the Examiner is respectfully requested to telephone the undersigned at telephone number (212) 808-0700 so that the issue(s) might be promptly resolved.

CONDITIONAL PETITION FOR EXTENSION OF TIME

If entry and consideration of the amendments above requires an extension of time, Applicants respectfully request that this be considered a petition therefor. The Assistant Commissioner is authorized to charge any fee(s) due in this connection to Deposit Account No. 14-1263.

ADDITIONAL FEE

Please charge any insufficiency of fees, or credit any excess, to Deposit Account No. 14-1263.

Respectfully submitted,

NORRIS McLAUGHLIN & MARCUS, P.A.

By _____

Paul Lim
Attorney for Applicant(s)
Reg. No. 55,383
875 Third Avenue - 18th Floor
New York, New York 10022
Phone: (212) 808-0700
Fax: (212) 808-0844